

Appendix A

Appendix A: Cassava's Allegations of Falsity as to Bredt & Pitt's Defamatory Statements

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Information available to the petitioner, however, which is summarized below and detailed in the enclosed technical report, raise grave concerns about the quality and integrity of the laboratory-based studies surrounding this drug candidate and support the claims for its efficacy.	Cassava is a fraud.	Ex. 3, 8/18/21 Citizen Petition Letter ("CPL") at 1 FAC ¶161(a)	¶¶162–167
Petitioner has enclosed with this Petition (and incorporates herein) a detailed technical report presenting multiple reasons to question the quality and integrity of the research supporting Cassava's claims about Simufilam's use for Alzheimer's Disease.	Cassava is a fraud.	Ex. 3, 8/18/21 CPL at 2 FAC ¶161(b)	¶¶162–167
Petition submits that the extensive evidence set forth in the enclosed report, which presents grave concerns about the quality and integrity of the scientific data supporting Cassava's claims for Simufilam's efficacy, provides compelling grounds for pausing the ongoing clinical trials until the FDA can conduct and complete a rigorous audit of Cassava's research.	Cassava is a fraud.	Ex. 3, 8/18/21 CPL at 2 FAC ¶161(c)	¶¶162–167

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Statement of Concern Regarding the Accuracy and Integrity of Clinical and Preclinical Data Supporting the Ongoing Clinical Evaluation of Compound PTI-125, Also Known As Simufilam	Cassava is a fraud.	Ex.3, 8/18/21 Citizen Petition Report ("CPR") at Cover FAC ¶161(d)	¶¶162–167
This report raises concerns about the quality and integrity of the laboratory-based studies surrounding this drug candidate.	Cassava is a fraud.	Ex. 3, 8/18/21 CPR at 1 FAC ¶161(e)	¶¶162–167

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>This letter details a long-standing pattern of seemingly intentional data manipulation and misrepresentation in scientific papers and corporate disclosures authored primarily by Drs. Hoau-Yan Wang, Associate Medical Professor, City University of New York, and Lindsay A Burns, Sr. Vice President of Neuroscience at Cassava Sciences. All the information detailed herein was obtained from public, non-proprietary sources. These apparent falsifications have helped garner [over] \$5,000,000 in NIH grants for preclinical/clinical studies, attract [over] \$250,000,000 in public fundraising by Cassava Sciences and misdirect therapeutic studies for patients suffering from Alzheimer's Disease. In the interest of the safety of patients with Alzheimer's disease enrolled in Cassava Sciences' ongoing clinical trials, as well as the NIH and other stakeholders, the biomedical and financial communities must be made aware of these apparent falsehoods.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 3, 8/18/21 CPR at 3–4 FAC ¶161(f)</p>	<p>¶¶162–167</p>
<p>Consequently, we investigated the published journal articles and other public sources of data underlying the development of simufilam in greater detail. This initial analysis suggests a pattern of clear errors and anomalies that are consistent with data manipulation and misrepresentation.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 3, 8/18/21 CPR at 4 FAC ¶161(g)</p>	<p>¶¶162–167</p>

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<p>Cassava Science apparently didn't get the Theranos memo. Their desire to do groundbreaking scientific research doesn't give the company and its executives a get out of jail free card from regulators, patients or investors. All stakeholders are entitled to nothing less than the complete truth about what its drug could do today, not what the company hoped it might do someday.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 3, 8/18/21 Dunn Letter at 1 FAC ¶161(h)</p>	<p>¶¶162–167</p>
<p>No other lab has confirmed Cassava's research connecting Filamin A to AD, nor has any other lab confirmed that Simufilam binds or modifies Filamin A or has effects in AD models. This presents a real problem because the company's own research is riddled with red flags. In the accompanying report, we provide extensive details regarding our many concerns about the accuracy and integrity of clinical and preclinical data supporting the ongoing clinical evaluation of Simufilam. The errors and anomalies occur in a pattern that is frequently favorable to Cassava's hypotheses and is of a sufficient frequency and magnitude to strongly suggest scientific misconduct.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 3, 8/18/21 Dunn Letter at 1 FAC ¶161(i)</p>	<p>¶¶162–167</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>In my initial petition, I provided extensive documentation regarding my clients many concerns about the accuracy and integrity of Drs. Wang and Burns' clinical and preclinical data supporting ongoing clinical evaluation of Simufilam, as well as the Company's own clinical data analyses. Due to the numerous serious red flags associated with their foundational research, I formally requested that you halt two ongoing trials of the drug (NCT04388254 and NCT04994483), pending a thorough audit by the FDA of the matters described therein.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPL at 1 FAC ¶161161(j)</p>	<p>¶¶162–167</p>
<p>Over the last two weeks, publicly and privately, the scientific community has validated many of my clients concerns and identified countless new errors and anomalies that strongly suggest scientific misconduct in their reports about both preclinical and clinical data.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPL at 1 FAC ¶161(k)</p>	<p>¶¶162–167</p>
<p>Supplemental Statement of Concern Regarding the Accuracy and Integrity of Clinical and Preclinical Data Supporting the Ongoing Clinical Evaluation of Compound PTI-125, Also Known as Simufilam.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPL at Cover Page FAC ¶161(l)</p>	<p>¶¶162–167</p>

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<p>In my Citizen Petition, specifically our technical summary exhibit (Technical Summary), we noted our concerns about possible data manipulation in both preclinical and clinical studies from Cassava. We believe the pre-clinical data concerns we raised completely undercut the foundational data for a role for filamin A in Alzheimer's disease (AD) and for any efficacy of Simufilam for treating AD.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPL at 1 FAC ¶161(m)</p>	<p>¶¶162–167</p>
<p>As you know, on 8/18/21, I filed an FDA whistleblower submission with you and a related Citizen's Petition with the Division of Dockets Management. In these filings, I provided extensive documentation regarding my clients many concerns about the accuracy and integrity of clinical and preclinical data supporting the ongoing clinical evaluation of Simufilam.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPR Attachment FAC ¶161(n)</p>	<p>¶¶162–167</p>
<p>Accordingly, my whistleblower clients would like to report to you their numerous concerns about the accuracy and integrity of clinical and preclinical data supporting the FDA's ongoing evaluation of Simufilam. The attached report demonstrates an unmistakable pattern of errors and anomalies that consistently favor Cassava's hypotheses and is of a sufficient frequency and magnitude to strongly suggest serious scientific misconduct.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 4, 8/30/21 CPR Attachment FAC ¶161(o)</p>	<p>¶¶162–167</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
In my Citizen Petition and first supplemental submission, we noted concerns about possible data manipulation in both preclinical and clinical studies associated with Simufilam.	Cassava is a fraud.	Ex. 5, 9/9/21CPR at 1 FAC ¶161(p)	¶¶162–167
Things aren't always as they appear. Things that aren't right can be made to look right. And, tragically, my clients' worst fears about Cassava Sciences appear to have been true.	Cassava is a fraud.	Ex. 9, 11/17/21 CPL at 1 FAC ¶161(xx)	¶¶162–167
Increasingly, evidence suggests that Cassava has doctored its research and clinical trial results, duped peer-reviewed journals, used the tainted science to trick the NIH and FDA into approving grants and clinical trials, misled investors by touting their grants and clinical trials without disclosing their troubling research practices, and withheld material information about the true nature of its drug from vulnerable Alzheimer's Disease patients.	Cassava is a fraud.	Ex. 9, 11/17/21 CPL at 1 FAC ¶161(yy)	¶¶162–167
As detailed in our original Citizen's Petition and in subsequent filings, including this one, the major concerns of my clients relate to the apparent manipulation of clinical data by Cassava.	Cassava is a fraud.	Ex. 9, 11/17/21 CPL at 1 FAC ¶161(zz)	¶¶162–167

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<p>On November 3, 2021, Quintessential Capital released a public report that raises new and serious questions about Cassava Sciences and its drug candidate simufilam. . . Following an in-depth investigation, among other things, the firm found that Cassava's clinical trials were administered by several controversial and questionable characters, that there were irregularities in the manner that the simufilam trials were conducted, and that the reported results of Cassava's clinical trials appear to have been manipulated—in various ways.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 9, 11/17/21 CPL at 3 FAC ¶161(aaa)</p>	<p>¶¶162–167</p>
<p>On the same date, a coalition of four scientists released a public presentation . . . and report . . . that both mirrored and expanded upon the numerous serious concerns about the accuracy and integrity of clinical and preclinical data outlined in our Citizen's Petition. Specifically, among other significant things, the authors . . . reported that Cassava Sciences and Dr. Hoau-Yan Wang appear to have fabricated pre-clinical and clinical evidence across the entire simufilam program, provided inadequate and unreliable safety studies for simufilam, and engaged in serious misconduct in the analysis of and reporting of clinical trial data—particularly the drug's much touted cognitive outcomes.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 9, 11/17/21 CPL at 3-4 FAC ¶161(bbb)</p>	<p>¶¶162–167</p>

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<p>Since the filing of the Citizen's Petition, publicly and privately, the scientific community has validated many of my clients' concerns and identified countless new errors and anomalies that are consistent with scientific misconduct in Cassava Sciences' reports about both preclinical and clinical data.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 9, 11/17/21 CPL at 8 FAC ¶161(ccc)</p>	<p>¶¶162–167</p>
<p>The nature and extent of these anomalies strongly suggest systematic data manipulation and misrepresentation because they frequently favor the authors' hypotheses and are outside of the scientific norm.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 9, 11/17/21 CPL at 8 FAC ¶161(ddd)</p>	<p>¶¶162–167</p>
<p>As detailed in my Citizen's Petition and in subsequent filings, including this one, their major concern relates to the mounting evidence that Cassava Sciences has doctored its research and clinical trial results to dupe peer-reviewed journals and to trick the FDA into approving its clinical trials.</p>	<p>Cassava is a fraud.</p>	<p>Ex. 11, 12/8/21 CPL at 1 FAC ¶161(fff)</p>	<p>¶¶162–167</p>
<p>Given the many obvious problems with the underlying research, to protect vulnerable Alzheimer's patients, the current clinical trial should be paused while a rigorous audit of Cassava's research is conducted.</p>	<p>Cassava has not tested for safety.</p>	<p>Ex. 3, 8/18/21 Dunn Letter at 2 FAC ¶168(a)</p>	<p>¶¶169–173</p>

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<p>If this true, the FDA as a continuing duty to carefully assess the safety and effective [sic] of Simufilam, based on the scientific research relied upon by Cassava Sciences. And this research rises and falls completely on the controversial work of Dr. Hoau-Yan Wang and Dr. Lindsay Burns, the wife of Remi Barbier, the President and CEO of the company.</p>	<p>Cassava has not tested for safety.</p>	<p>Ex. 4, 8/30/21 CPL at 1 FAC ¶168(b)</p>	<p>¶¶169–173</p>
<p>With these significant concerns, my clients remain skeptical about the entirety of Cassava's clinical data, including the safety data, which may also have been manipulated.</p>	<p>Cassava has not tested for safety.</p>	<p>Ex. 9, 11/17/21 CPL at 1 FAC ¶168(o)</p>	<p>¶¶169–173</p>
<p>It is worth repeating, the preclinical and clinical foundations linking Filamin A to Alzheimer's disease derive only from publications of Drs. Wang and Burns. As show above, ALL of these papers have evidence of apparent intentional scientific misrepresentation.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 3, 8/18/21 CPR at 18 FAC ¶174(a)</p>	<p>¶¶175–178</p>
<p>NIH and CUNY should audit the publications and lab of Dr. Wang to determine the existence and extent of data manipulation and fraud in all papers and grant applications from Drs. Wang and Burns.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 3, 8/18/21 CPR at 19 FAC ¶174(b)</p>	<p>¶¶175–178</p>

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<p>Since our last supplemental submission, new analysis by my clients and other independent scientists raises serious concerns about Cassava's foundational claims for the binding of PTI-125 to filamin A and, separately, the methodology and reporting about their diagnostic test for Alzheimer's Disease, SavaDX, which is a key end point [for] two [of] Cassava's Phase 3 trials (NCT04994483 and NCT05026177).</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 11, 12/8/21 CPL at 1 FAC ¶174(k)</p>	<p>¶¶175–178</p>
<p>In our Citizen's Petition, we stated that this figure [figure 1B] is suspicious/implausible because of (1) the improbably high 570 femtomolar affinity and (2) the gradual increase in binding that span 6 log changes (10⁻¹³ to 10⁻⁷ M) of PTI-125. . . Our recent re-inspection of the Methods section for this crucial experiment shows seemingly irrefutable evidence of data manipulation/fabrication.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 11, 12/8/21 CPL at 2 FAC ¶174(l)</p>	<p>¶¶175–178</p>
<p>Assuming one [C14] as is likely, Cassava's claimed specific activity for PTI-125 is ~1000 times higher than theoretically possible. Such an inexplicable error would create insurmountable problems and invalidate the study.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 11, 12/8/21 CPL at 3 FAC ¶174(m)</p>	<p>¶¶175–178</p>

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<p>These issues underscore the implausibility of claiming to measure 580 fM binding affinity with C-14 labeled simufilam. Indeed, the numerous elementary problems with Cassava's experiments raise troubling questions about whether simufilam binds to filamin A at all.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 11, 12/8/21 CPL at 6 FAC ¶174(n)</p>	<p>¶¶175–178</p>
<p>It is important to note that no other labs have replicated this alleged potent interaction. Fatal flaws in these critical binding experiments, which form the foundation for their key investigations, raise serious questions about Cassava's hypotheses [sic] that filamin A is relevant to Alzheimer's disease and about whether simufilam affects filamin A.</p>	<p>Cassava relies upon fabricated and manipulated foundational research.</p>	<p>Ex. 11, 12/8/21 CPL at 6 FAC ¶174(o)</p>	<p>¶¶175–178</p>
<p>The underlying papers of Drs. Wang and Burns involve extensive use of Western blot analyses to support their claims connecting Simufilam to Alzheimer's. Detailed analysis of the western blots in the published journal articles shows a series of anomalies that are suggestive of systematic data manipulation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPL at 2 FAC ¶179(a)</p>	<p>¶¶180–188</p>

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<p>The integrity of western blot analysis: Western blotting was extensively used by Drs. Wang and Burns over the past 15 years to support their foundational scientific claims and underscores their SavaDx clinical plasma biomarker. Detailed analysis of the western blots in the published journal articles from Drs. Wang and Burns shows a series of anomalies. The extent of these anomalies forms a 15-year pattern that strongly suggests systematic data manipulation and misrepresentation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 2 FAC ¶179(b)</p>	<p>¶¶180–188</p>
<p>The western blot data presented by Wang and Burns are almost always overexposed and highly processed, which has been repeatedly seen in previously reported examples of image manipulation. In the following sections, we present a series of examples with strong evidence of image manipulation. In the appendix, we include additional examples which raise red flags.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 7 FAC ¶179(c)</p>	<p>¶¶180–188</p>
<p>This degree of congruence could not have occurred by chance or error; it suggests a complex cross-publication dimension to Cassava Science's band duplication behavior and, in this case, it is hard to imagine that the duplication was not intentional.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 9 FAC ¶179(d)</p>	<p>¶¶180–188</p>

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<p>In their 2008 paper PLoS ONE 3:e1554, Drs. Wang and Burns again present a series of overexposed and selectively cropped gels that appear to show spliced experiments (i.e., two separate experiments combined as if they were done simultaneously). . . The similarity in these images could not have occurred by chance.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 10 FAC ¶179(e)</p>	<p>¶¶180–188</p>
<p>The foundational paper from Drs. Wang and Burns that links Filamin A and PTI 125 to Alzheimer's disease is The Journal of Neuroscience, 2012 32:9773–9784. This paper appears to contain a collection of questionable western blots. Most of the paper comprises western blots that are of low quality, over exposed and selectively cropped. In this paper, the authors appear to have duplicated and transposed bands. There are dozens of questionable image features in this paper, only a small sampling is presented here. Numerous additional examples of this pattern of behavior in other manuscripts are included in the appendix.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 11 FAC ¶179(f)</p>	<p>¶¶180–188</p>
<p>In Figure 1a the four Filamin A bands in the top set are more similar to each than can be expected by chance and appear to be duplicates. . . this degree of misalignment is suspicious.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 11 FAC ¶179(g)</p>	<p>¶¶180–188</p>

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Figure 6b: The four rightmost bands appear to be identical to each other. This degree of similarity is unlikely to occur by chance.	Cassava relies upon fabricated and manipulated western blots.	Ex. 3, 8/18/21 CPR at 12 FAC ¶179(h)	¶¶180–188
Figure 11a: The five leftmost tau bands appear to be identical to each other, AND the 3 rightmost tau bands appear to be identical to each other. These degrees of similarity are unlikely to occur by chance.	Cassava relies upon fabricated and manipulated western blots.	Ex. 3, 8/18/21 CPR at 12 FAC ¶179(i)	¶¶180–188
There are many other examples that strongly suggest data manipulation in this Journal of Neuroscience paper. Individually, each of these examples is concerning, but together they form a pattern that strongly calls into question the integrity of this publication (and the other publications from these authors with similar patterns of band insertion).	Cassava relies upon fabricated and manipulated western blots.	Ex. 3, 8/18/21 CPR at 13 FAC ¶179(j)	¶¶180–188

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<p>In summary, it appears that Drs. Wang and Burns in published PubMed indexed manuscripts and through disclosures with Cassava Sciences have misrepresented preclinical and clinical research results for more than 15 years. This initial examination of their published western blots identified many dozens of examples of protein bands that appear to have been duplicated and/or misrepresented, a Western blot that was used twice to represent different experimental conditions, and a normalization blot that appears to have been manually constructed.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 18 FAC ¶179(k)</p>	<p>¶¶180–188</p>
<p>The volume of problematic material uncovered in publicly available sources indicates a thorough audit would likely unveil significant additional scientific misconduct and data manipulation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 18 FAC ¶179(l)</p>	<p>¶¶180–188</p>
<p>The congruence of these oddly shaped bands are [sic] unlikely to have occurred by chance and raises the possibility of band duplication and data manipulation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 30 FAC ¶179(m)</p>	<p>¶¶180–188</p>
<p>The uncanny resemblance of these “battleship” shaped bands and the precise alignment of the dot artifacts suggests that one or both were intentionally inserted, perhaps with the intention of misrepresenting the results.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 31 FAC ¶179(n)</p>	<p>¶¶180–188</p>

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<p>Once can see that four Filamin A bands in the bottom set of Figure 1A appear to be identical to each other. This degree of similarity is unlikely to occur by chance, and the thin white borders surrounding each band could be due to merging multiple images in a photo editing software.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 32 FAC ¶179(o)</p>	<p>¶¶180–188</p>
<p>Figure 12A (below) of the Journal of Neuroscience paper, used human Alzheimer's disease tissue to establish the SavaDx biomarker and effects of PTI-125/simufilam. The ten filamin A (FLNA) bands appear identical in size and shape. As protein bands on Western blots typically have unique features, ten consecutive indistinguishable bands are exceedingly unlikely to occur by chance and were probably manually duplicated.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 33 FAC ¶179(p)</p>	<p>¶¶180–188</p>
<p>A subsequent paper alleging to connect PTI-125 with Alzheimer's disease is 2017 Neurobiol Aging 55:99–114. Again, this paper largely comprises a series of overexposed, and apparently manipulated and cropped Western blots. Band duplication appears to occur throughout this paper. . . The similarity in size and share of the bands in the purple boxes seemingly could not have occurred by chance. This and many other blots in this paper appear to have been manipulated.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 34 FAC ¶179(q)</p>	<p>¶¶180–188</p>

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<p>The following example of a manipulated western blot occurred earlier than the examples referenced in the primary document. Dr. Wang was the first author of this 2022 paper in <i>Journal of Biological Chemistry</i> 278:P31547–32553 and it is one of the few examples presented in this document without Dr. Burns as a co-author. The apparent manipulation applied to this blot is similar to that shown in C2.2.1.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 35 FAC ¶179(r)</p>	<p>¶¶180–188</p>
<p>Because of the contemporaneous examples of western blot manipulation, we undertook an evaluation of the author's highest profile publication, a 2006 publication in <i>Nature Medicine</i> 12:824–828. . . There are numerous suspicious appearing blots in this publication, as well.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 36 FAC ¶179(s)</p>	<p>¶¶180–188</p>
<p>Importantly, there is clearly a smooth background between the two dark bands and a textured background only behind the dark bands. This was not likely done for cosmetic reasons, it strongly suggests a manufactured/fraudulent result. There is no legitimate explanation for this pattern of findings.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 3, 8/18/21 CPR at 39 FAC ¶179(t)</p>	<p>¶¶180–188</p>

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<p>As we noted in the Technical Summary, analysis of published journal manuscripts shows a series of anomalies that suggest a 15-year pattern of systematic data manipulation and misrepresentation in virtually every publication underlying Cassava's Simufilam claims. Many of our specific claims have now been independently validated by others, including Dr. Bik, and posted on PubPeer. Specifically, these include a total of 8 papers by Dr. Wang, including 4 papers co-authored with Dr. Burns, noted to have apparent image manipulation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 4, 8/30/21 CPR at 8 FAC ¶179(u)</p>	<p>¶¶180–188</p>
<p>In addition to confirming the Western blot data manipulations we detailed in the Technical Summary, Dr. Bik noted multiple other Western blot data examples that appeared to show data manipulation.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 4, 8/30/21 CPR at 10 FAC ¶179(v)</p>	<p>¶¶180–188</p>
<p>Dr. David Vaux, deputy director of science integrity and ethics at the Australian Walter and Eliza Hall of Medical Research stated: "It is not conceivable that features in the images (such as apparent duplications) arose due to coincidence (chance) or accident, leaving the only plausible explanation being that the images were deliberately falsified or fabricated."</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 4, 8/30/21 CPR at 10 FAC ¶179(w)</p>	<p>¶¶180–188</p>

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<p>A major problem with this is that international leaders in the nAChR field agree that there are no antibodies suitable for Western blotting of alpha7 nAChR in the brain. . . Therefore, the alpha7 nACHR data that form a mechanistic foundation for simufilam seem scientifically undoable. This fundamental limitation for alpha7 nACHR Western blotting raises serious questions regarding the validity of Fig. 1A, Fig. 2A, Fig. 9A, Fig. 10A, and Fig. 12A in Cassava's 2012 Journal of Neuroscience paper--the very same paper that Cassava heavily touted in a recent process release as having only one "human error."</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 9, 11/17/21 CPL at 4 FAC ¶179(bb)</p>	<p>¶¶180–188</p>
<p>In the end, all their purported alpha7 nAChR Western blotting research in the brain is seemingly undoable.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 9, 11/17/21 CPL at 5 FAC ¶179(cc)</p>	<p>¶¶180–188</p>
<p>This seemingly irrefutable data manipulation is important both because it implies a pattern of reckless scientific misconduct and because it undercuts foundational science related to simufilam mechanism of action in Alzheimer's disease.</p>	<p>Cassava relies upon fabricated and manipulated western blots.</p>	<p>Ex. 9, 11/17/21 CPL at 14 FAC ¶179(dd)</p>	<p>¶¶180–188</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Some of the foundational studies published by Drs. Wang and Burns make claims about Simufilam's effects in experiments conducted on postmortem human brain tissue. The methodology allegedly used in these experiments defies logic, and the data presented again have hallmarks of manipulation.	Cassava relies upon fabricated and manipulated testing using human brain tissue.	Ex. 3, 8/18/21 CPL at 2 FAC ¶189(a)	¶¶190–196
The integrity of analyses involving human brain tissue: Simufilam is reported to bind to its target and modify a range of downstream molecules in experiments conducted on post-mortem human brain tissue from subjects with Alzheimer's disease and neurological controls. . . The complex, multi-step cellular processes the authors claim to observe in tissue that has been dead for a decade are contrary to a basic understanding of neurobiology. As with the western blot data, there are anomalies in the presentation of the data which again strongly suggest manipulation.	Cassava relies upon fabricated and manipulated testing using human brain tissue.	Ex. 3, 8/18/21 CPR at 2 FAC ¶189(b)	¶¶190–196
It is unlikely that the enzyme responsible for phosphorylation would survive the initial -80°C freezing step. Moreover, the phosphorylation experiments are reported to have been performed at 4°C, but it is unlikely that the enzyme responsible for phosphorylation would be active at 4°C (enzymes generally work best a body temperature--37°C).	Cassava relies upon fabricated and manipulated testing using human brain tissue.	Ex. 3, 8/18/21 CPR at 14 FAC ¶189(c)	¶¶190–196

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>The age and post-mortem interval for the groups of subjects are the same (down to the decimal points) in each of the three papers. It is therefore reasonable to assume the same human brain specimens were used across the studies from 2008-2017, so the results are premised on the enzymes in the human brain extracts remaining active up to 13 hours post-mortem before freezing, remaining active after nearly 10 years in frozen archival without any advanced cryopreservative techniques, and being active at 4° C.</p>	<p>Cassava relies upon fabricated and manipulated testing using human brain tissue.</p>	<p>Ex. 3, 8/18/21 CPR at 15 FAC ¶189(d)</p>	<p>¶¶190–196</p>
<p>The complex, multi-step cellular process the authors claim to observe in tissue that has been dead for a decade are contrary to a basic understanding of neurobiology. . . As with the western blot data, there are anomalies in the presentation of the data from this human tissue, which again strongly suggest manipulation.</p>	<p>Cassava relies upon fabricated and manipulated testing using human brain tissue.</p>	<p>Ex. 3, 8/18/21 CPR at 15–16 FAC ¶189(e)</p>	<p>¶¶190–196</p>
<p>Finally, the methodology alleged used to evaluate the function of simufilam in postmortem brain tissue defies logic and the data presented again have clear hallmarks of manipulation.</p>	<p>Cassava relies upon fabricated and manipulated testing using human brain tissue.</p>	<p>Ex. 3, 8/18/21 CPR at 19 FAC ¶189(f)</p>	<p>¶¶190–196</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Six further aspects of the research by Drs. Wang and Burns are incompatible with scientific norms, and these claims raise further suspicions.	Additional So-Called "Suspensions" Regarding Cassava's Research.	Ex. 3, 8/18/21 CPL at 3 FAC ¶197(a)	¶¶198–203
In the appendix, six additional areas of concern are raised. These frequent errors and anomalies occur in a pattern which is frequently favorable to the authors' hypotheses and is of sufficient magnitude to strongly suggest scientific misconduct. This scientific work is foundational to the link between simuflam and its supposed target Filamin A in AD.	Additional So-Called "Suspensions" Regarding Cassava's Research.	Ex. 3, 8/18/21 CPR at 2–3 FAC ¶197(b)	¶¶198–203
Six further aspects of the research by Drs. Wang and Burns are incompatible with scientific norms, and these claims raise further suspicions. These issues are enumerated below. In addition to many examples of apparent Western blot manipulation and clinical data misreporting noted above, a number of additional western blots are included at the end of this appendix which raise additional red flags.	Additional So-Called "Suspensions" Regarding Cassava's Research.	Ex. 3, 8/18/21 CPR at 21 FAC ¶197(c)	¶¶198–203

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
In the Technical Summary, we noted six further aspects of the research by Drs. Wang and Burns that are incompatible with scientific norms and that raise further suspicions. As follow up to our Citizen Petition to the FDA, the scientific community provided strong support for many of our suspicions . . .	Additional So-Called "Suspicious" Regarding Cassava's Research.	Ex. 4, 8/30/21 CPR at 11 FAC ¶197(d)	¶¶198–203
Suspicious Claim #1: Remarkably High Affinity Bonding Between PTI-125 and Filamin A	Additional So-Called "Suspicious" Regarding Cassava's Research.	Ex.3, 8/18/21 CPR at 21 FAC ¶197(e)	¶¶198–203
Figure 1b in this paper [Neurobiology of Aging 2017; 55:99-114] also shows that PTI-125 displacement occurs over 7 orders of magnitude. This "shallow" displacement is highly unusual/unprecedented. An experienced pharmacologist could advise that this is suspicious/implausible.	Additional So-Called "Suspicious" Regarding Cassava's Research.	Ex. 3, 8/18/21 CPR at 21 FAC ¶197(f)	¶¶198–203
Suspicious Claim #2: Remarkably High Affinity Bonding Between Naloxone and Filamin A	Additional So-Called "Suspicious" Regarding Cassava's Research.	Ex. 3, 8/18/21 CPR at 22 FAC ¶197(h)	¶¶198–203

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Also unusual is the “shallow” displacement curve in figure 3 [in <i>PLOS One</i> 2008; 3:e1554 paper] that spans 4-5 orders of magnitude. An experienced opiate receptor pharmacologist could advise that this figure is suspicious/implausible.	Additional So-Called “Suspicious” Regarding Cassava’s Research.	Ex. 3, 8/18/21 CPR at 22 FAC ¶197(i)	¶¶198–203
Suspicious Claim #3: Isoelectric Focusing Experiments in Multiple Papers Indicate 100% of Filamin in Altered Conformation in Alzheimer’s Disease and largely Restored to Correct Conformation by PTI-125	Additional So-Called “Suspicious” Regarding Cassava’s Research.	Ex. 3, 8/18/21 CPR at 23 FAC ¶197(j)	¶¶198–203
Second, isoelectric focusing gels do not typically “look” like the image below. Especially for a 290 kD protein like Filamin A, one would not expect such a crisp bands in isoelectric focusing. An experienced biochemist could advise that this figure is suspicious/implausible. This is especially suspect considering the apparent pattern of band manipulation by Drs. Wang and Burns on Western blots.	Additional So-Called “Suspicious” Regarding Cassava’s Research.	Ex. 3, 8/18/21 CPR at 23 FAC ¶197(k)	¶¶198–203
Suspicious Claim #5: PTI-125/Simufilam Improves Memory in a Mouse Model of Alzheimer’s Disease	Additional So-Called “Suspicious” Regarding Cassava’s Research.	Ex. 3, 8/18/21 CPR at 25 FAC ¶197(m)	¶¶198–203

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>In <i>Neurobiol Aging</i> 2017; 55L99-114, figure 9 show a pre-clinical study of simufilam in a mouse model of AD and misrepresents the data as showing “improvements in memory.” It is dubious that any legitimate experiment approximating the methodology described could yield the reported results. . . A mouse neurobehavioral specialist would likely advise that there are significant problems with all of the behavioral and memory data presented in the paper. Importantly, this is the only pre-clinical cognitive/memory data that has been published supporting simufilam's efficacy as a cognitive enhancer.</p>	<p>Additional So-Called “Suspensions” Regarding Cassava's Research.</p>	<p>Ex. 3, 8/18/21 CPR at 25-26 FAC ¶197(n)</p>	<p>¶¶198–203</p>
<p>Suspicious Claim #6: PTI-125/Simufilam Blocks the Interaction Between β-amyloid and α7-Nicotinic Acetylcholine Receptors</p>	<p>Additional So-Called “Suspensions” Regarding Cassava's Research.</p>	<p>Ex. 3, 8/18/21 CPR at 27 FAC ¶197(o)</p>	<p>¶¶198–203</p>
<p>In the Technical Summary, we noted that the femtomolar affinity claimed by Cassava for PTI-125 binding to Filamin A is suspiciously high and seemingly implausible. We also noted that no other group has confirmed this remarkable claim.</p>	<p>Additional So-Called “Suspensions” Regarding Cassava's Research.</p>	<p>Ex. 4, 8/30/21 CPR at 11 FAC ¶197(d)</p>	<p>¶¶198–203</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Since our presentation, Dr. Bik has flagged an isoelectric focusing gel in Neurobiology of Aging 2017 55:99-114 as having a band that “appears to be surrounded by a rectangle of a different background than the rest of the blot,” which suggests it was manipulated confirming our suspicions around the authenticity of Cassava’s isoelectric focusing gels [].</p>	<p>Additional So-Called “Suspensions” Regarding Cassava’s Research.</p>	<p>Ex. 4, 8/30/21 CPR at 11–12 FAC ¶197(l)</p>	<p>¶¶198–203</p>
<p>Since the petition was made public, Dr. Bik noted that a histologic micrograph (microscopic brain tissue picture) in that Wang et al. Journal of Neuroscience paper that was alleged stained with anti-A β42 looks suspiciously similar to a different brain tissue picture that was allegedly stained with an antibody to Neurofilament. She implied that the same brain section was differentially cut and pasted to reflect different experimental treatments and would confirm our suspicions regarding the invalidity of their β-amyloid antibody-based experiments.</p>	<p>Additional So-Called “Suspensions” Regarding Cassava’s Research.</p>	<p>Ex. 4, 8/30/21 CPR at 12 FAC ¶197(p)</p>	<p>¶¶198–203</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Cassava's presentation of clinical biomarker data from the Phase 2b trials raises questions about the validity of the data. The CSF samples in this study were first analyzed by an outside lab, which found that Simufilam was ineffective in improving the primary biomarkers. But Cassava had these sample analyzed again and this time reported that Simufilam rapidly and robustly improved a wide array of biomarkers. Cassava has not fully published the data from this reanalysis, but a presentation poster that it published on July 26, 2021, which appears to describe aspects of that work, shows signs of data anomalies or manipulation.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 3, 8/18/21 CPL at 3 FAC ¶210(a)</p>	<p>¶¶211–214</p>
<p>The validity of clinical biomarker data: Biomarker analysis from patients treated with simufilam in Cassava's double-blind study forms a primary basis for Cassava's claim that simufilam engages its target in the central nervous system, but there are concerns about the integrity of this data.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 3, 8/18/21 CPR at 1 FAC ¶210(b)</p>	<p>¶¶211–214</p>
<p>This re-analysis showed that simufilam rapidly and robustly improved a wide array of CSF biomarkers. Whereas Cassava has not fully published this reanalysis, Cassava's 26 July 2021 poster presumably describing aspects of that work shows signs of data manipulation.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 3, 8/18/21 CPR at 2 FAC ¶210(c)</p>	<p>¶¶211–214</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Second, plasma biomarker data from these same patients, which were just presented by Cassava Sciences, contains evidence of manipulation. If there's no biomarker signal, and there is apparent misrepresentation of clinical data[,] the continuation of the ongoing Cassava trials may put patients at risk without the claimed evidence of biomarker benefit.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 3, 8/18/21 CPR at 6 FAC ¶210(d)</p>	<p>¶¶211–214</p>
<p>The underlying data for these results have been deposited by the Company on ClinicalTrials.gov [] and do not support the data provided in the CTAD presentation. This initial analysis was provided by Jesse Brodtkin on Twitter [].</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 4, 8/30/21 CPR at 5 FAC ¶210(e)</p>	<p>¶¶211–214</p>
<p>Many of the results from Dr. Wang's Phase 2b redo have what appear to be data manipulation or GROSS LAB ERRORS—values incompatible with standards for these types of analyses—which raises additional questions about the validity of the biomarker results associated with the redo.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Reanalysis Manipulation.</p>	<p>Ex. 5, 9/9/21 CPR at 2 FAC ¶210(f)</p>	<p>¶¶211–214</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Note that the change from Day 1 in total errors (ClinicalTrials.gov) does not match the data in the CTAD presentation. Further, the 50 mg treatment group demonstrated a greater difference than the 100 mg treatment group. An additional concern is that any analysis of change between treatment and placebo appears to be compromised by inequivalent baseline measurements.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Biomarker Data.</p>	<p>Ex. 4, 8/30/21 CPR at 6 FAC ¶215(a)</p>	<p>¶¶216–221</p>
<p>If the missing value for the 100 mg treatment group [] is inserted, the p-value changes from the Company's reported value of ~0.01 to a non-significant p-value of 0.08. They hypothesize that the missing +150% value from the 100 mg group was moved to the placebo group. . . Because the study evaluated multiple biomarkers, neither of these group would be considered statistically different from placebo when accounting for multiple comparison.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Biomarker Data.</p>	<p>Ex. 4, 8/30/21 CPR at 7 FAC ¶215(b)</p>	<p>¶¶216–221</p>
<p>Of the ten biomarkers analyzed, it seems the baselines for three are far outside expectations. As these baselines are mean averages from 60+ patients, their extreme variation from many other Alzheimer's Disease (AD) biomarker studies suggests the redo has major lab errors or manipulation.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Biomarker Data.</p>	<p>Ex. 5, 9/9/21 CPR at 5 FAC ¶215(c)</p>	<p>¶¶216–221</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
In our September 9th supplement, we noted that three of the ten biomarkers analyzed by Dr. Wang and presented by Cassava in the phase 2b study of simufilam in Alzheimer's disease had baseline values so far outside expectations that they suggest lab errors or manipulation.	Cassava fabricated and manipulated its Phase 2b Study: Biomarker Data.	Ex. 9, 11/17/21 CPL at 5 FAC ¶215(t)	¶¶216–221
In the Technical Summary, we listed our concerns about Company's statements regarding the initial and subsequent analysis of the original Phase 2b data. Specifically, we noted that the Company was not transparent regarding the "re-do" analysis of the Phase 2b data.	Cassava fabricated and manipulated its Phase 2b Study: Outside Lab.	Ex. 4, 8/30/21 CPR at 2 FAC ¶227(a)	¶¶228–230

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>This is a MAJOR problem for two reasons. First, Wang is a long-time member of Cassava's Scientific Advisory Board one of its principal paid scientific consultants and its lead scientist reasonable for the Company's Simufilam research, so his secretly conducting the redo contradicts Cassava's key public statements, including the September 2020 press release and 2020 form 10-K, which stated that the samples were sent to outside labs for bioanalysis. Second, the scientific community has identified countless red flags that call into question the accuracy and integrity of Wang's research. In fact, some scientific integrity experts (see below) have suggested that most of his published research has data that appears to be "deliberately falsified or fabricated."</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Outside Lab.</p>	<p>Ex. 4, 8/30/21 CPR at 3 FAC ¶227(b)</p>	<p>¶¶228–230</p>
<p>In its September 14, 2020 press release and 2020 Form 10-K at page 12, Cassava stated that the redo was conducted by an "outside lab." Contrary to these public statements and filings, the Research Square preprint [] documenting Cassava's redo analysis states that the experiments were done by Dr. Wang and associates at CUNY.</p>	<p>Cassava fabricated and manipulated its Phase 2b Study: Outside Lab.</p>	<p>Ex. 5, 9/9/21 CPR at 3 FAC ¶227(c)</p>	<p>¶¶228–230</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Our Technical Summary highlighted potential image manipulation in the analysis of the Company's Phase 2a clinical data, which we originally identified in the above referenced 8-K filing of 5 December 2019.</p>	<p>Cassava fabricated and manipulated its Phase 2a Study.</p>	<p>Ex. 4, 8/30/21 CPR at 3 FAC ¶231(a)</p>	<p>¶¶232–238</p>
<p>Additionally, since dissemination of the Citizen Petition, other scientists have investigated this publication and others. Specifically, Dr. Elisabeth Bik, a former Stanford University scientist and the world's best-known detective of image manipulation in scientific publications, confirmed our analysis of this image in a common on PubPeer. She expressed major concerns with the integrity of these phase 2a data and advised the inspection of the original images is needed to assess the authenticity of the clinical study results.</p>	<p>Cassava fabricated and manipulated its Phase 2a Study.</p>	<p>Ex. 4, 8/30/21 CPR at 4 FAC ¶231(b)</p>	<p>¶¶232–238</p>
<p>On September 3, 2021, Remi Barbier, Cassava's CEO, claimed in a public statement "we don't have the original films or images for the Western blots in question. Those were generated by our science collaborator at CUNY, who is Prof. Wang." However, this representation is highly doubtful.</p>	<p>Cassava fabricated and manipulated its Phase 2a Study.</p>	<p>Ex. 5, 9/9/21 CPR at 2 FAC ¶231(c)</p>	<p>¶¶232–238</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>These apparent biomarker discrepancies are so extreme that they suggest lab errors or manipulation. It is worth noting that Cassava's publication of these suspicious Phase 2a biomarker data occurred in a paper (JPAD 2020 4:256) that was accepted just 6 days after submission, which calls into question the credibility and rigor of that journal's peer review process.</p>	<p>Cassava fabricated and manipulated its Phase 2a Study.</p>	<p>Ex. 9, 11/17/21 CPL at 6 FAC ¶231(f)</p>	<p>¶¶232–238</p>
<p>In their phase 2b open label study of simufilam in Alzheimer's disease, Cassava claims improvement in patient's cognition. Careful evaluation of patient baseline cognition scores shows peculiarities that raise significant concerns about their interpretation of the data. Critical analyses of these results are posted on Twitter . . . and we incorporate aspects of those analyses below.</p>	<p>Cassava fabricated and manipulated its Open Label Study.</p>	<p>Ex. 9, 11/17/21 CPL at 6 FAC ¶239(l)</p>	<p>¶¶240–245</p>
<p>There are two red flags with these reported data. First, the observed mean ADAS-Cog 11 scores after 6 and 9 months are virtually the same (13.9 vs. 13.6, respectively), so the data do not appear to demonstrate a continued improvement. Second, the baseline data between the 6-month and 9-month analyses changes substantially, and to a degree that seems inconsistent with other information provided by the company, suggesting possible manipulation.</p>	<p>Cassava fabricated and manipulated its Open Label Study.</p>	<p>Ex. 9, 11/17/21 CPL at 7 FAC ¶239(m)</p>	<p>¶¶240–245</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
Cassava's Phase 3 Special Protocol Assessment (SPA) for Simufilam was supported by preclinical studies and phase 2a and 2b biomarker studies. For the many reasons enumerated in my original Citizen's Petition and the two supplemental submissions, we strongly believe countless such false and misleading statements have been made by Cassava Sciences.	Cassava lied to FDA for Phase 3 Studies.	Ex. 5, 9/9/21 CPR at 8 FAC ¶246(a)	¶¶247–251
Suspicious Claim #4: Novel Blood Diagnostic SavaDx Represents Plasma Filamin A Level	Cassava lied about SavaDX.	Ex. 3, 8/18/21 CPR at 24 FAC ¶252(a)	¶¶253–257
Owing to how large (290kD) proteins run on gels, an experienced biochemist would advise that the blots in figure 2 [from Cassava Sciences' July 26, 2021 poster] likely do not represent the 290kD protein Filamin A. . . Considering all of the apparently manipulated western blots in papers from Drs. Wang and Burns, this is particularly suspect.	Cassava lied about SavaDX.	Ex. 3, 8/18/21 CPR at 24 FAC ¶252(b)	¶¶253–257
As there is not a single gold standard for diagnosing AD, it seems highly improbable that any test could have 98-100% accuracy.	Cassava lied about SavaDX.	Ex. 11, 12/8/21 CPL at 7 FAC ¶252(e)	¶¶253–257

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
For these and other reasons, Cassava's assertions about SavaDX seem implausible and have been largely ignored for years by the neuroscience community.	Cassava lied about SavaDX.	Ex.11, 12/8/21 CPL at 7–8 FAC ¶252(f)	¶¶253–257
Suddenly pausing SavaDx is another major red flag, as Cassava has described it has fast and inexpensive.	Cassava lied about SavaDX.	Ex.11, 12/8/21 CPL at 10 FAC ¶252(g)	¶¶253–257
For these and other reasons, we believe Cassava paused SavaDx and has begun to lower expectations because the problems with SavaDX have been exposed or feared would soon be exposed.	Cassava lied about SavaDX.	Ex.11, 12/8/21 CPL at 10 FAC ¶252(h)	¶¶253–257
Furthermore, potentially powerful, and direct evidence of data manipulation related to SavaDx was documented on 29 November 2021 by a group of scientists independently investigating Cassava. They posted their concerns, of which we were previously unaware, on Twitter. . . They also made a PDF of the presentation available online at SAVA Dx: Theranos 2.0 (cassavafraud.com).	Cassava lied about SavaDX.	Ex.11, 12/8/21 CPL at 10 FAC ¶252(i)	¶¶253–257
Several apparent red flags arise when comparing the raw data in the FOIAed email with the figures in Cassava's AAIC poster.	Cassava lied about SavaDX.	Ex.11, 12/8/21 CPL at 11 FAC ¶252(j)	¶¶253–257

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>Like Tesla and Elon Musk's use of Twitter, Cassava Sciences and Remi Barbier regularly get into trouble with their press releases. As illustrated by their 9/14/20 press release that falsely claimed that a different academic lab conducted the redo (and increased the company's share price by 133.4%), or the misleading 8/26/21 press release in which the company tried to use Quanterix as an alibi for its alleged misconduct, they tend to make misleading statements in an effort to exonerate themselves or boost the company's flagging share price.</p>	<p>Cassava's Executives Engage in Insider Trading.</p>	<p>Ex.9, 11/17/21 CPL at 16–17 FAC ¶273(f)</p>	<p>¶¶274–280</p>
<p>Based on a closer review of Cassava's press release [on 11/4/21], we suggest that it contains material misrepresentation or omissions. As a preliminary matter, if contacted by law enforcement or regulatory authorities, we are confident that the editors of the Journal of Neuroscience will state that the authorized statement did not constitute an endorsement or exoneration of any kind.</p>	<p>Cassava's Executives Engage in Insider Trading.</p>	<p>Ex.9, 11/17/21 CPL at 17 FAC ¶273(g)</p>	<p>¶¶274–280</p>

Bredt and Pitt's Defamatory Statement	False & Defamatory Message	FDA Filing & FAC Citation	FAC Falsity Citation
<p>The bottom line is Cassava Science does not appear to have provided the Journal of Neuroscience “original, uncropped Western blots” as represented in its 11/4/2021 press release, so the journal could not have exonerated them, as they so dramatically suggested. Making matters far worse, the company appears to have knowingly taken the published image (the one on the left above), blurred it a bit, and then photoshopped it onto a slightly different canvas to “create” the image on the right. Undoubtedly, these apparently deceptive acts were not disclosed to the Journal of Neuroscience, and countless investors were misled, as is evidenced by the market capitalization of Cassava Sciences almost doubling on this press release.</p>	<p>Cassava's Executives Engage in Insider Trading.</p>	<p>Ex.9, 11/17/21 CPL at 22 FAC ¶273(h)</p>	<p>¶¶274–280</p>